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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,730	11/28/2000	Paul D. Grossman	443D1	7771

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EXAMINER
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ART UNIT	PAPER NUMBER
1634	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/724,730	Applicant(s) GROSSMAN, PAUL D.	
	Examiner Juliet C. Einsmann	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is written in response applicant's correspondence submitted 2/7/02, paper number 11. Claims 1-11 have been amended. Claims 1-12 are pending. Applicant's amendments and arguments have been thoroughly reviewed but are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. THIS ACTION IS FINAL.

Claim Rejections - 35 USC § 102

2. Claims 1, 2, 3, 5, 8, 9, 10, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Grossman *et al.* (US 5514543).

Grossman *et al.* (US 5514543) teach a composition comprising:

a first complex comprising a first probe comprising a first target specific portion for sequence specific hybridization to a first target nucleic acid, and a first tag; and a first mobility modifier comprising a first tail and a first tag complement for binding the first tag and

a second complex comprising a second probe comprising a second target specific portion for sequence specific hybridization to a second target nucleic acid, and a second tag; and a second mobility modifier comprising a second tail and a second tag complement for binding the second tag,

wherein a mobility of the first complex in a mobility-dependent analysis technique is distinguishable from a mobility of the second complex in the mobility-dependent analysis technique; and wherein the first complex and the second complex are present in a mixture. For an example of the basic structure of the complexes, see, for example, Figure 1A. The

polynucleotide marked (22) is the tag complement. The portion marked (27) is the tail, which is made of a polymer, for example polyethylene oxide or a polypeptide chain (Col. 3, lines 59-61). The portion marked (24) is the tag (in this case shown bound to the tag complement). The portion of (26) which is not hybridized to the tag complement is the target specific portion, and this portion would inherently comprise a 3'-hydroxyl group. Grossman *et al.* teach that their method is for the detection of a "plurality of selected target sequences (Col. 3, line 1)" and thus, a plurality of these complexes would exist in a mixture.

Grossman *et al.* exemplify a tag and tag complement which comprise the sequence TCC (Fig. 4A). The compositions taught by Grossman *et al.* include probe elements attached to a polymer chain which imparts a distinctive electrophoretic mobility in a sieving matrix to the associated probe pair (Col. 3, lines 6-10). In one embodiment the compositions taught by Grossman *et al.* include tails made of polyethyleneoxide units (Col. 8, lines 33-34). Furthermore, Grossman *et al.* teach compositions which include hybridization enhancers, such as magnesium chloride (Col. 28, line 40, for example).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman *et al.* (US 5514543) in view of Buchardt *et al.* (Trends in Biotechnology (1993) 11(9):384-6).

Grossman *et al.* teach a composition comprising:

a first complex comprising a first probe comprising a first target specific portion for sequence specific hybridization to a first target nucleic acid, and a first tag; and a first mobility modifier comprising a first tail and a first tag complement for binding the first tag and

a second complex comprising a second probe comprising a second target specific portion for sequence specific hybridization to a second target nucleic acid, and a second tag; and a second mobility modifier comprising a second tail and a second tag complement for binding the second tag,

wherein a mobility of the first complex in a mobility-dependent analysis technique is distinguishable from a mobility of the second complex in the mobility-dependent analysis technique; and wherein the first complex and the second complex are present in a mixture. For an example of the basic structure of the complexes, see, for example, Figure 1A. The polynucleotide marked (22) is the tag complement. The portion marked (27) is the tail, which is made of a polymer, for example polyethylene oxide or a polypeptide chain (Col. 3, lines 59-61). The portion marked (24) is the tag (in this case shown bound to the tag complement). The portion of (26) which is not hybridized to the tag complement is the target specific portion, and this portion would inherently comprise a 3'-hydroxyl group. Grossman *et al.* teach that their method is for the detection of a "plurality of selected target sequences (Col. 3, line 1)" and thus, a plurality of these complexes would exist in a mixture.

Grossman *et al.* do not teach a composition in which the first tag complement portion comprises PNA.

Buchardt *et al.* teach PNA probes and teach that PNA probes were found to form very stable Watson-Crick duplexes with DNA and RNA and that the affinity for PNAs for DNA and RNA is generally higher that that of the corresponding DNA for DNA or RNA (p. 385).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have substituted PNA for the tag complement taught by Grossman *et al.* The ordinary practitioner would have been motivated to make such a combination by the teachings of both Grossman *et al.* and Buchardt *et al.* Grossman *et al.* teaches that the sequence specific binding polymer (herein designated as the tag complement portion) is "a polymer effective to bind one target nucleic acid or sequence subset with base-sequence specificity (Col. 6, lines 6-8)," and Buchardt *et al.* teach that PNA probes have such qualities. Buchardt *et al.* further teach benefits of using PNA probes in place of DNA structures, stating that "PNAs exhibit sequence-specific binding to DNA and RNA with higher affinities and specificities than unmodified DNA. They are resistant to nuclease and protease attack in serum and cellular extracts and, thus, appear very promising as diagnostic and biomolecular probes (Abstract)."

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 4-10, 13, and 15-18 of copending Application No. 09/232000 in view of Grossman *et al.* (US 5514543).

The claims of the co-pending application are drawn to compositions which comprise a first probe comprising a first target specific portion and a first tag (called a clamp specific portion) and a first mobility modifier (the clamp) comprising a first tail (second probe specific portion or the label) and a first tag complement for binding to the first tag (first probe specific portion). The co-pending claims do not specifically teach compositions in which the label is a results in distinguishable mobility, nor do they teach compositions which comprise a plurality of these compositions.

Grossman *et al.* (US 5514543) teach compositions useful for detecting multiple sequences in a single assay. The compositions taught by Grossman *et al.* include probe elements attached to a polymer chain which imparts a distinctive electrophoretic mobility in a sieving matrix to the associated probe pair (Col. 3, lines 6-10). In one embodiment the compositions taught by Grossman *et al.* include tails made of polyethyleneoxide units (Col. 8, lines 33-34). Grossman *et al.* teach that these compositions are useful in methods to provide multiple probe-target complexes where the probe-complexes are resolved in a mobility-dependent analysis technique (Col. 2, line 66-Col. 3, line 12). Grossman *et al.* further teach labels attached to probes (See for example, Col. 9, lines 60-65).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have combined the methods claimed in the '000 application with the mobility modifiers taught by Grossman *et al.* The ordinary practitioner would have been motivated to make such a substitution because Grossman *et al.* expressly teaches that the use of mobility modifiers "allows a plurality of target sequences to be assayed in a single-assay format, with rapid identification of sequences according to the mobilities of different polymer chains associated with the sequence-specific labeled probes. The polymer chains allow for separation of single and double stranded oligonucleotides, in a simple chromatography or electrophoresis method. In particular, the method allows for effective fractionation of a plurality of oligonucleotides, all of which have similar or identical sizes (Col. 22, lines 35-43)." Thus the combination of the teachings of Grossman *et al.* with the claims of the '000 application would have resulted in a method that allows for the effective interrogation of a plurality of oligonucleotides.

This is a provisional obviousness-type double patenting rejection.

Response to Remarks

Applicant points out that in Grossman, element 26 (designated in the office action as comprising the tag and target specific portions) is defined as the target nucleic acid sequence itself. However, this is irrelevant to the instant inquiry. The fact that Grossman defines this element as a "target sequence" does not remove that fact that it comprises a portion that is capable of sequence-specific binding to a target nucleic acid sequence (the definition of target specific portion in the instant specification). Applicant's arguments essentially directed towards the intended use of the probe as defined herein and that as defined in the Grossman reference. A

recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In the instant case, the instantly claimed complexes are no different from those disclosed by Grossman (see MPEP 2111.02).

No arguments were provided regarding the provisional double patenting rejection.

Conclusion

7. No claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C Einsmann
Examiner
Art Unit 1655

May 1, 2002